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## Descriptive Epidemiology of Nonsyndromic Complete Atrioventricular Canal Defects

A. J. Agopian<sup>a</sup>, Mousumi Mouluk<sup>b</sup>, Monesha Gupta-Malhotra<sup>b</sup>, Lisa K. Marengo<sup>c</sup>, and Laura E. Mitchell<sup>a,\*</sup>

<sup>a</sup>Center for Human Genetics, Division of Epidemiology, Human Genetics and Environmental Sciences, University of Texas School of Public Health, Houston, Texas

<sup>b</sup>Division of Cardiology, Department of Pediatrics, University of Texas Medical School, Houston, Texas

<sup>c</sup>Birth Defects Epidemiology and Surveillance Branch, Texas Department of State Health Services, Austin, Texas

### Abstract

**Background**—Complete atrioventricular canal defects (CAVC) are a common heart defect, but few epidemiologic studies have evaluated nonsyndromic CAVC. Risk factors for nonsyndromic CAVC have not been well established.

**Methods**—To assess the relationship between risk for nonsyndromic CAVC in offspring and several sociodemographic and reproductive parental factors, including maternal diabetes and obesity, we conducted Poisson regression analyses, using data ascertained through the Texas Birth Defects Registry, a large, population-based birth defects registry. Data were evaluated for 563 nonsyndromic cases with CAVC.

**Results**—Significant associations were observed between nonsyndromic CAVC in offspring and maternal pregestational diabetes (adjusted prevalence ratio (aPR): 6.74, 95% confidence interval (CI): 3.67–12.37), gestational diabetes [aPR: 1.69, 95% CI: 1.03, 2.79], and obesity [aPR: 1.69, 95% CI: 1.24, 2.30].

**Comments**—Our findings add nonsyndromic CAVC to the growing list of birth defects that appear to be associated with maternal diabetes and obesity.

### INTRODUCTION

Birth defects are a leading cause of infant mortality.<sup>1</sup> Further, congenital heart defects are the leading cause of birth defect-related mortality and the etiology of heart defects is poorly understood.<sup>2</sup> Heart defects represent a heterogeneous group of malformations, and some types of heart defects have been better studied than others. Complete atrioventricular canal defects (CAVC) are the most common type of endocardial cushion defect, and involve deficiencies of the endocardial cushion-derived components of the atrial and ventricular septae and a single common atrioventricular valve ring. CAVC represents approximately 3% of heart defects, occurring in two per 10,000 live births.<sup>3</sup> More than 50% of CAVC occur in conjunction with trisomy 21, and 50% of infants with untreated CAVC, whether syndromic or nonsyndromic, will die during the first year of life.<sup>3, 4</sup> Few epidemiologic studies have

Correspondence: Laura E. Mitchell, Ph.D., University of Texas School of Public Health, 1200 Herman Pressler Dr., Houston, TX 77030, laura.e.mitchell@uth.tmc.edu, Phone: 713-500-9954, Fax: 713-500-9958.

evaluated nonsyndromic CAVC and risk factors for nonsyndromic CAVC have not been well established.

Maternal pregestational diabetes, gestational diabetes, and obesity are independently associated with increased risk for birth defects, including heart defects, in offspring.<sup>5, 6</sup> Since more than one-third of adult women in the US are obese or diabetic, and the prevalence of each is rising,<sup>7, 8</sup> it is important to delineate the full range of adverse outcomes associated with maternal obesity and diabetes. Although animal models suggest that maternal diabetes may increase offspring risk for CAVC,<sup>9</sup> the effects of maternal obesity, diabetes, or other factors on offspring risk for CAVC have not been well studied in humans. Therefore, we conducted a descriptive epidemiologic study of CAVC, evaluating the possible influence of a wide range of sociodemographic and reproductive factors, including maternal diabetes and obesity, on risk for CAVC.

## METHODS

### Study Population

We conducted descriptive analyses using CAVC data from the Texas Birth Defects Registry. This registry is maintained by the Birth Defects Epidemiology and Surveillance Branch (BDESB) at the Texas Department of State Health Services.<sup>10</sup> Active case surveillance is used to identify live births, fetal deaths, and induced pregnancy terminations with birth defects. Cases are included in the registry when the mother resides in Texas at the time of delivery and a diagnosis of a structural malformation or developmental disability is made within the first year of delivery. Case data are abstracted from medical records at all birthing centers, delivery hospitals, midwife facilities, and pediatric hospitals in Texas by BDESB staff. Diagnoses are classified using a six-digit code defined by the Centers for Disease Control and Prevention, based on the British Pediatric Association Classification of Diseases and the International Classification of Diseases, 9<sup>th</sup> Revision, Clinical Modification system (BPA code).<sup>11</sup> Case data from medical records are then linked to sociodemographic and reproductive data from birth and fetal death certificates from the Texas Vital Statistics Unit of the Texas Department of State Health Services.

The present analyses included cases from the registry with documented postnatal confirmation of diagnoses of endocardial cushion defects (BPA code 745.6) from 1999–2008, including cases that were live births, fetal deaths, and induced pregnancy terminations. Main analyses focused on those cases with CAVC (BPA code 745.620). Data were available for maternal variables (maternal age at delivery, race/ethnicity, history of previous live births, history of previous pregnancies that did not result in live births, onset of prenatal care during the first trimester [yes versus no], education level, birthplace, residence in a county bordering Mexico, residence type [e.g., rural], marital status at time of delivery, pregestational diabetes, gestational diabetes, and prepregnancy body mass index), paternal variables (paternal age at delivery and race/ethnicity), and case variables (delivery year, season of conception, plurality of the pregnancy, and sex). Residence type was defined based on county population size (i.e., rural urban continuum code), as described by Langlois et al.<sup>12</sup> Season of conception was based on month of last menstrual period and was categorized as winter (December–February), spring (March–May), summer (June–August), and fall (September–November). Information on overall presence or absence of maternal diabetes, regardless of pregestational or gestational onset, was available for the entire study period. Specific information on maternal pregestational diabetes, gestational diabetes, and prepregnancy body mass index (BMI) was only available for deliveries in 2005–2008. Data on type of pregestational diabetes (i.e., type 1 versus type 2) were not available. For all of these variables, data from vital records were used; however, when data were missing or when a vital record was not available for a case, data abstracted from medical records were

used to determine: maternal age at delivery, race/ethnicity, history of previous live births, residence in a county bordering Mexico, and residence type, and infant sex, plurality, and year of delivery. In order to make comparisons, vital records data were obtained from the Texas Vital Statistics unit of the Texas Department of State Health Services for all live births in Texas during the study period.<sup>13</sup> The protocol for this study was approved by the Institutional Review Board for the University of Texas Health Science Center at Houston.

## Statistical Methods

We conducted descriptive analyses to identify sociodemographic or reproductive characteristics that may increase risk for CAVC. First, we tabulated frequencies of cases with syndromic and nonsyndromic endocardial cushion defects, including CAVC. Syndromic cases were defined as cases with possible or confirmed diagnoses of a chromosome abnormality or malformation syndrome or sequence, based on BPA codes. Patients with visceral heterotaxy were included in the nonsyndromic group. To limit heterogeneity, all subsequent analyses were conducted among cases with nonsyndromic CAVC. Among these nonsyndromic cases, frequencies of additional major birth defects, including heterotaxy, were determined.

We estimated birth prevalence and crude prevalence ratios using data from cases in the numerator and data from all live births in the denominator. Poisson regression was used to estimate prevalence ratios. Variables that were available for the entire study period and were significantly associated ( $p < 0.05$ ) or associated with borderline significance (i.e., lower 95% confidence interval limit  $> 0.99$  for positive associations or upper 95% confidence limit

$< 1.01$  for negative associations) with nonsyndromic CAVC in crude analyses were included in the main multivariable model. Multivariable analyses were repeated for deliveries during 2005–2008, using the maternal gestational diabetes, pregestational diabetes, and BMI variables instead of the overall diabetes variable. For this analysis, we included all other variables in the original multivariable model. All analyses were performed using SAS (version 9.1 copyright 2002–2008, SAS, Inc., Cary, NC).

Visceral heterotaxy has been associated with maternal pregestational diabetes and is often observed in conjunction with CAVC.<sup>5, 14</sup> Therefore, analyses for 2005–2008 deliveries and the full study period were also repeated among cases without heterotaxy, to ensure that any observed associations were independent of associations with heterotaxy. Further, analyses for the full study period were also repeated among a small subset of cases with isolated CAVC (i.e., those without any additional major [cardiac or non-cardiac] birth defects).

## RESULTS

There were 3,806,299 total live births and 1,588 total cases with documented postnatal diagnoses of endocardial cushion defects from 1999–2008 (Table 1). There were 1,335 cases with CAVC; therefore, the total prevalence of CAVC was 3.51 per 10,000 live births. The majority of cases with CAVC (58%) had chromosome abnormalities or malformation syndromes (Table 1), the most common being trisomy 21 (52%,  $N=693$ ). Cases with heterotaxy syndrome were included under nonsyndromic CAVC (NSCAVC). Subsequent analyses focused on cases with NSCAVC ( $N=563$ ). The prevalence of NSCAVC was 1.48 per 10,000 live births.

The proportion of cases with NSCAVC that were live births, fetal deaths, and induced terminations were 98.6%, 0.4%, and 1.1%, respectively. There were two fetal deaths and six induced terminations. Associated major birth defects in the NSCAVC cases are presented by system or structure in Table 2 (and defined in Supplementary Table 1). Heterotaxy syndrome was present in 38.7% ( $N=218$ ) of the NSCAVC cases. Additional congenital

heart defects commonly reported in the NSCAVC cases included persistent left superior vena cava (25.4%, N=143), transposition of the great vessels (39.4%, N=222), persistent right aortic arch (19%, N=107), ostium secundum atrial septal defect (32.5%, N=183), hypoplastic left ventricle (18.5%, N=104), total anomalous pulmonary venous return (18.5%, N=104), and hypoplastic right ventricle (8.0%, N=45).

The variables that were significantly associated with NSCAVC in offspring in the main crude analyses (i.e., for the entire study period) were maternal age, paternal age, marital status, plurality, and maternal diabetes (i.e., pregestational or gestational) (Table 3). These variables were all included in the main multivariable model (Table 4). A significantly increased prevalence of NSCAVC in offspring was seen among women who were not married at time of delivery compared to those who were married [adjusted prevalence ratio (aPR): 1.31, 95% confidence interval (CI): 1.03, 1.66]. In addition, the prevalence of NSCAVC in offspring was also increased among women with diabetes (pregestational or gestational) compared to those without diabetes [aPR: 2.63, 95% CI: 1.87, 3.70].

To further explore the relationship between maternal diabetes and NSCAVC in offspring, we repeated analyses using data only from 2005–2008, which included maternal gestational diabetes, pregestational diabetes, and BMI variables (Table 4). In the multivariable model, a significantly increased prevalence of NSCAVC in offspring was observed among women with pregestational diabetes [aPR: 6.74, 95% CI: 3.67, 12.37] or gestational diabetes [aPR: 1.69, 95% CI: 1.03, 2.79] as well as among obese (i.e., BMI  $\geq 30$  kg/m<sup>2</sup>) women [aPR: 1.69, 95% CI: 1.24, 2.30], compared to women without these conditions.

Because heterotaxy in offspring has previously been associated with maternal diabetes,<sup>5</sup> we repeated analyses among 345 cases without heterotaxy, and in these analyses, similar magnitudes of associations with diabetes and obesity were observed (Table 4). Further, a similar magnitude of association with diabetes was observed in analyses repeated for the full study period among the 47 cases with isolated CAVC (Table 4). Analyses were not repeated for 2005–2008 among cases with isolated CAVC because there were only 18 such cases during this period.

## DISCUSSION

The overall prevalence of CAVC in the present study was similar to that reported in previous studies.<sup>15, 16</sup> Further, the distribution of syndromes among cases with syndromic CAVC was similar to previous reports, as was the distribution of additional major birth defects among nonsyndromic cases.<sup>14, 15</sup>

Maternal pregestational diabetes is a known risk factor for congenital heart defects overall, as well as for several specific subtypes of congenital heart defects (e.g. conotruncal defects and heterotaxia).<sup>5, 17–20</sup> However, many previous studies have been limited by small numbers of cases with specific congenital heart defect subtypes. Due to the rarity of nonsyndromic CAVC, potential risk factors, including maternal diabetes, have not been well studied in relation to nonsyndromic CAVC.

In the present study, we found an increased prevalence of nonsyndromic CAVC in offspring of women with pregestational diabetes, gestational diabetes, obesity (BMI  $\geq 30$ ), or unmarried marital status at delivery. We are aware of only one other study that evaluated the descriptive epidemiology of nonsyndromic CAVC.<sup>14</sup> In that study, based on data from the National Birth Defects Prevention Study (N=122 cases), a lower prevalence of CAVC was seen in offspring of Hispanic mothers [crude PR: 0.4, 95% CI: 0.2, 0.7].<sup>14</sup> A similar association was not observed in the present study, which used a study population with more than five times as many cases with Hispanic mothers. Although a borderline significant

higher prevalence of CAVC was seen among multiple compared to single gestation pregnancies in the present study [aPR: 1.6, 95% CI: 1.0, 2.5] (Table 4), the prevalence among multiple gestation pregnancies was not significantly increased in data from the National Birth Defects Prevention Study [crude PR: 1.1, 95% CI: 0.4, 2.8].<sup>14</sup>

Significant associations have been reported between pregestational (but not gestational) maternal diabetes and isolated [adjusted OR: 12.4, 95% CI: 3.7, 41.5] and non-isolated [OR: 25.3, 95% CI: 4.2, 152.1] atrioventricular septal defects in data from the National Birth Defects Prevention Study (N=85 cases).<sup>5</sup> An association between pregestational diabetes and atrioventricular septal defects has also been reported in data from the EUROCAT registry after adjustment for maternal age, year, and registry [adjusted OR: 2.2, 95% CI: 1.2, 4.0].<sup>21</sup> Atrioventricular septal defects and CAVC have also been evaluated in data from the Baltimore-Washington Infant Study, and significant crude associations between pregestational diabetes and CAVC have been reported in analyses involving a small number of cases [N=31 cases, OR: 22.8, 95% CI: 7.4, 70.5].<sup>4, 22, 23</sup> To our knowledge, an association between gestational diabetes and CAVC has not been previously reported.

The association between pregestational diabetes and complex heart defects involving conotruncal septation, cardiac looping, or the endocardial cushion (as reported in our study) points towards an early teratogenic effect on cardiac development (weeks 3–8) by an abnormal metabolic milieu in diabetic mothers.<sup>20, 24</sup> The biologic basis for the association between maternal gestational diabetes, which is typically diagnosed after the first trimester, and CAVC is difficult to explain and may reflect cases of undiagnosed pregestational diabetes mellitus diagnosed as gestational diabetes.<sup>17, 25</sup>

Several previous studies have reported associations between prepregnancy maternal elevated BMI or obesity and offspring risk for heart defects overall, as well as specific heart defects (e.g., left ventricular outflow tract defects, conotruncal defects).<sup>26–28</sup> However, maternal obesity and CAVC has not been well studied and, to our knowledge, this is the first report of a statistically significant association between maternal obesity and CAVC. Three studies have, however, reported non-significant, elevated associations between elevated BMI and atrioventricular septal defects [adjusted ORs: 1.8, 1.4, and 1.2].<sup>6, 26, 27</sup>

The novel association between CAVC in offspring and maternal unmarried status may reflect underlying involvement of additional unknown socioeconomic or behavioral factors. Unmarried status has been associated with other adverse pregnancy outcomes in Texas,<sup>29</sup> and similar associations between unmarried status and heart defects overall in offspring have been reported<sup>30, 31</sup> but the relationship between marital status and heart defects has not been thoroughly evaluated.

The present study had limitations. Data for maternal obesity, pregestational diabetes, and gestational diabetes was only available for more recent years (i.e., 2005–2008). Similar to other studies of diabetes and birth defects,<sup>5, 23</sup> information on type of pregestational diabetes (i.e., type 1 or type 2), diabetes severity, glycemic control, method of diabetes diagnosis, and clinical confirmation of diagnosis was not available. Data for pregestational, gestational, and overall maternal diabetes and obesity were collected from vital records for cases and all livebirths. It seems likely that maternal diabetes and obesity could be underreported on vital records;<sup>32</sup> however, the observed prevalence of gestational diabetes, pregestational diabetes, and obesity from 2005–2008 among all live births (i.e., 3.7%, 0.6%, and 20.8%, respectively, data not shown) seems reasonably similar to previous estimates (e.g., 2–10%, 0.5%, and 22%, respectively).<sup>5, 33–35</sup> Further, previously reported associations between maternal diabetes or obesity and other heart defects support our findings. We cannot rule out



the presence of unmeasured confounding by other factors, as our analyses were limited to available data.

There are several strengths to this study, including use of a population-based, multiracial/ethnic sample ascertained by an active surveillance system that includes both liveborn and non-liveborn cases. To our knowledge, this descriptive study contains the largest sample of cases with CAVC described in the literature. We attempted to limit heterogeneity by restricting our case definition to a subset of endocardial cushion defects (i.e., CAVC), and by restricting analyses to nonsyndromic cases. Results for our subgroup analyses also support the main results, and suggest that maternal diabetes and obesity increase offspring risk for CAVC independently of heterotaxy.

In summary, we have identified maternal factors that may increase risk for CAVC. The observed associations between CAVC in offspring and maternal pregestational diabetes, gestational diabetes, and obesity seem consistent with previous findings. Further research is indicated to confirm our findings and better understand the biological mechanisms that underlie these associations.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table 1**

Distribution of Endocardial Cushion Defects and Specified Syndromic and Nonsyndromic Subgroups.

Endocardial cushion defect type and subgroup	N (%)
CAVC <sup>a</sup>	1,335
Syndromic	772 (57.8)
Trisomy 21	693 (51.9)
Trisomy 18	31 (2.3)
Trisomy 13	10 (0.7)
Other chromosome abnormalities	16 (1.2)
Other syndromes	33 (2.5)
Nonsyndromic	563 (42.2)
Additional cardiac or non-cardiac malformation	516
Additional cardiac malformation only	223
Visceral heterotaxy	218
Isolated CAVC <sup>a</sup>	47
CAVC <sup>a</sup> and single or hypoplastic ventricle variants	287
Trisomy 21	49 (17.1)
Nonsyndromic	221 (77.0)
Ostium primum defects without CAVC <sup>a</sup>	143
Trisomy 21	34 (23.8)
Nonsyndromic	95 (66.4)
Single common atrium	106
Trisomy 21	3 (2.8)
Nonsyndromic	86 (81.1)
Other endocardial cushion defect	62
Trisomy 21	27 (43.5)
Nonsyndromic	30 (48.4)

<sup>a</sup> Complete atrioventricular canal defects

**Table 2**

Additional Major Birth Defects Among Nonsyndromic Cases with Complete Atrioventricular Canal Defects (N=563)

Major birth defect <sup>a</sup>	N	%
<b>Additional cardiovascular anomalies</b>		
Septal defects		
Additional ventricular septal defect	61	10.8
Secundum atrial septal defect	183	32.5
Conotruncal defects		
Tetralogy of Fallot	18	3.2
Pulmonary infundibular stenosis, not otherwise specified	56	9.9
Transposition of great vessels	222	39.4
Common truncus	8	1.4
Aortic arch abnormalities		
Coarctation of aorta	66	11.7
Hypoplasia of aorta	78	13.9
Persistent right aortic arch	106	18.8
Anomalies of great veins		
Persistent left superior vena cava	143	25.4
Total anomalous pulmonary venous return	104	18.5
Partial anomalous pulmonary venous return	20	3.6
Hypoplastic or single ventricle variants		
Hypoplastic left ventricle	104	18.5
Hypoplastic right ventricle	45	8.0
Hypoplastic ventricle, not otherwise specified	5	0.9
Single ventricle, not otherwise specified	67	11.9
Additional specified abnormality of common atrioventricular valve		
Congenital stenosis of 'mitral' component	71	12.6
Atresia or stenosis of 'tricuspid' component	25	4.4
Anomalies of aortic valve		
Congenital stenosis of aortic valve	30	5.3
Congenital insufficiency of aortic valve	1	0.2
Anomalies of pulmonary valve		
Atresia, hypoplasia, or absence of pulmonary valve	75	13.3
Stenosis of pulmonary valve	83	14.7
Unspecified pulmonary atresia, stenosis, or hypoplasia	58	10.3
Anomalies of pulmonary artery	148	26.3
Anomalies of coronary artery or sinus	32	5.7
<b>Additional non-cardiac birth defects</b>		
Visceral heterotaxy	218	38.7
Anomalies of nervous system	38	6.7
Anomalies of eye	10	1.8

Major birth defect <sup>a</sup>	N	%
Anomalies of ear, face, and neck	34	6.0
Anomalies of respiratory system	22	3.9
Anomalies of digestive system		
Anomalies of intestinal fixation	93	16.5
Anomalies of gallbladder, bile ducts, and liver	22	3.9
Other specified anomalies of stomach	62	11.0
Anomalies of urinary system and genital organs	76	13.5
Anomalies of musculoskeletal system		
Polydactyly	14	2.5
Anomalies of spine	29	5.2
Other anomalies of ribs and sternum	28	5.0

<sup>a</sup>Frequent additional major birth defects reported by system/structure

TABLE 3

Prevalence Estimates and Unadjusted Prevalence Ratios for Cases with Nonsyndromic Complete Atrioventricular Canal Defects in TX, 1999–2008

Variable	Cases (N=563)	Total live births (N=3,806,299)	Prevalence (/10,000 live births)	Unadjusted prevalence ratio [95% CI <sup>a</sup> ]
Maternal age (years)				
<20	79	538534	1.47	1.0 Reference
20–24	144	1070642	1.34	0.9 [0.7, 1.2]
25–29	149	1019564	1.46	1.0 [0.8, 1.3]
30–34	116	762017	1.52	1.0 [0.8, 1.4]
35–39	57	343776	1.66	1.1 [0.8, 1.6]
40	18	71377	2.52	1.7 [1.0, 2.9]
Paternal age (years) <sup>b</sup>				
<20	23	183310	1.25	1.0 Reference
20–24	84	683788	1.23	1.0 [0.6, 1.6]
25–29	124	872854	1.42	1.1 [0.7, 1.8]
30–34	106	783698	1.35	1.1 [0.7, 1.7]
35–39	72	458663	1.57	1.3 [0.8, 2.0]
40	54	267814	2.02	1.6 [1.0, 2.6]
Marital status				
Married	334	2442935	1.37	1.0 Reference
Unmarried	220	1360777	1.62	1.2 [1.0, 1.4]
Plurality				
Singleton	538	3695793	1.46	1.0 Reference
Multiple	25	110299	2.27	1.6 [1.0, 2.3]
Any diabetes				
Yes	48	131010	3.66	2.7 [2.0, 3.6]
No	503	3675287	1.37	1.0 Reference
Gestational diabetes <sup>c</sup>				
Yes	15	59597	2.52	1.6 [0.9, 2.7]
No	245	1537944	1.59	1.0 Reference
Pre-gestational diabetes <sup>c</sup>				
Yes	12	9690	12.38	7.9 [4.4, 14.2]
No	248	1587851	1.56	1.0 Reference
Body mass index (kg/m <sup>2</sup> ) <sup>c</sup>				
Underweight (<18.5)	9	72441	1.24	0.9 [0.5, 1.8]
Normal (18.5–24.9)	105	788537	1.33	1.0 Reference
Overweight (25.0–29.9)	70	393053	1.78	1.3 [1.0, 1.8]
Obese (≥ 30)	75	329813	2.27	1.7 [1.3, 2.3]
Previous live births				
No	222	1443081	1.54	1.0 Reference
Yes	340	2271640	1.50	1.0 [0.8, 1.2]

Variable	Cases (N=563)	Total live births (N=3,806,299)	Prevalence (/10,000 live births)	Unadjusted prevalence ratio [95% CI <sup>a</sup> ]
Previous pregnancies that did not result in live births				
No	428	2991926	1.43	1.0 Reference
Yes	119	754571	1.58	1.1 [0.9, 1.4]
Year of delivery				
1999	51	349157	1.46	1.0 Reference
2000	42	363325	1.16	0.8 [0.5, 1.2]
2001	49	365092	1.34	0.9 [0.6, 1.4]
2002	57	372369	1.53	1.1 [0.7, 1.5]
2003	43	377374	1.14	0.8 [0.5, 1.2]
2004	57	381441	1.49	1.0 [0.7, 1.5]
2005	55	385537	1.43	1.0 [0.7, 1.4]
2006	71	399309	1.78	1.2 [0.9, 1.7]
2007	63	407453	1.55	1.1 [0.7, 1.5]
2008	75	405242	1.85	1.3 [0.9, 1.8]
Sex				
Male	288	1945841	1.48	1.0 Reference
Female	275	1860458	1.48	1.0 [0.9, 1.2]
Maternal education				
>High school	199	1473279	1.35	1.0 Reference
High school	175	1109945	1.58	1.2 [1.0, 1.4]
<High school	173	1183477	1.46	1.1 [0.9, 1.3]
Maternal Residence (Texas-Mexico border)				
No	482	3318005	1.45	1.0 Reference
Yes	81	488294	1.66	1.1 [0.9, 1.4]
Maternal race/ethnicity				
Non-Hispanic white	205	1387934	1.48	1.0 Reference
Non-Hispanic black	67	424964	1.58	1.1 [0.8, 1.4]
Hispanic	280	1844103	1.52	1.0 [0.9, 1.2]
Paternal race/ethnicity <sup>c</sup>				
Non-Hispanic white	176	1222703	1.44	1.0 Reference
Non-Hispanic black	46	330461	1.39	1.0 [0.7, 1.3]
Hispanic	225	1563780	1.44	1.0 [0.8, 1.2]
Season of conception				
Winter	158	923181	1.71	1.0 Reference
Spring	122	873593	1.40	0.8 [0.6, 1.0]
Summer	117	849111	1.38	0.8 [0.6, 1.0]
Fall	150	916132	1.64	1.0 [0.8, 1.2]
First trimester prenatal care				
Yes	376	2696236	1.39	1.0 Reference
No	145	919749	1.58	1.1 [0.9, 1.4]

Variable	Cases (N=563)	Total live births (N=3,806,299)	Prevalence (/10,000 live births)	Unadjusted prevalence ratio [95% CI <sup>a</sup> ]
Residence type				
Metropolitan urbanized	502	3387886	1.48	1.0 Reference
Non-metropolitan urbanized	30	155328	1.93	1.3 [0.9, 1.9]
Less urbanized	31	263085	1.18	0.8 [0.6, 1.1]
Maternal birthplace <sup>d</sup>				
United States	148	922218	1.60	1.1 [0.9, 1.4]
Outside United States	132	921885	1.43	1.0 Reference
Total	563	3806299	1.48	

<sup>a</sup>CI, confidence interval

<sup>b</sup>Data were missing for 17.8% of cases for paternal age and 20.6% for paternal race/ethnicity

<sup>c</sup>Data available for cases delivered in 2005–2008 only

<sup>d</sup>Maternal birthplace was only analyzed among cases with Hispanic mothers



**TABLE 4**  
Adjusted Prevalence Ratios for Nonsyndromic Cases with Complete Atrioventricular Canal Defects in TX, 1999–2008

Variable	CAVC (N=563)			CAVC without heterotaxy (N=345)		Isolated CAVC (N=47)
	1999–2008 Adjusted prevalence ratio [95% CI <sup>a</sup> ]	2005–2008 Adjusted prevalence ratio [95% CI <sup>a</sup> ]	1999–2008 Adjusted prevalence ratio [95% CI <sup>a</sup> ]	2005–2008 Adjusted prevalence ratio [95% CI <sup>a</sup> ]	1999–2008 Adjusted prevalence ratio [95% CI <sup>a</sup> ]	
Maternal age (years)						
<20	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference	
20–24	1.0 [0.7, 1.5]	0.8 [0.5, 1.4]	1.3 [0.7, 2.4]	1.5 [0.6, 4.0]	0.6 [0.2, 1.7]	
25–29	0.9 [0.6, 1.5]	0.6 [0.4, 1.2]	1.2 [0.6, 2.4]	1.2 [0.4, 3.5]	0.1 [0.02, 0.4]	
30–34	0.9 [0.5, 1.5]	0.7 [0.4, 1.2]	1.2 [0.6, 2.6]	1.3 [0.4, 3.9]	0.1 [0.02, 0.5]	
35–39	0.9 [0.5, 1.6]	0.6 [0.3, 1.1]	1.3 [0.6, 2.9]	0.8 [0.2, 2.8]	0.1 [0.02, 0.9]	
40	1.4 [0.7, 2.9]	1.0 [0.4, 2.4]	2.1 [0.8, 5.7]	1.7 [0.4, 6.9]	-	
Paternal age (years) <sup>b</sup>						
<20	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference	
20–24	1.1 [0.6, 1.8]	1.1 [0.6, 2.2]	0.7 [0.3, 1.5]	0.6 [0.2, 1.9]	1.0 [0.2, 4.9]	
25–29	1.3 [0.7, 2.3]	1.3 [0.6, 2.7]	1.0 [0.4, 2.2]	1.0 [0.3, 3.2]	2.5 [0.5, 12.5]	
30–34	1.3 [0.7, 2.4]	1.6 [0.7, 3.4]	1.0 [0.4, 2.4]	1.2 [0.4, 4.3]	4.0 [0.7, 21.5]	
35–39	1.5 [0.8, 2.8]	2.0 [0.9, 4.5]	1.2 [0.5, 3.0]	1.9 [0.5, 6.9]	3.7 [0.6, 24.9]	
40	1.7 [0.9, 3.3]	2.3 [1.0, 5.3]	1.4 [0.5, 3.4]	2.1 [0.6, 8.0]	-	
Marital status						
Married	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference	
Unmarried	1.3 [1.0, 1.7]	1.4 [1.0, 1.8]	1.3 [0.9, 1.8]	1.5 [1.0, 2.3]	0.7 [0.3, 1.6]	
Plurality						
Singleton	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference	
Multiple	1.6 [1.0, 2.5]	1.7 [0.9, 2.9]	1.8 [1.0, 3.2]	1.6 [0.7, 3.8]	2.8 [0.7, 10.5]	
Any diabetes						
Yes	2.6 [1.9, 3.7]		3.1 [2.0, 4.7]		2.5 [0.7, 9.5]	
No	1.0 Reference		1.0 Reference		1.0 Reference	
Gestational diabetes <sup>c</sup>						
Yes		1.7 [1.0, 2.8]		2.0 [1.0, 4.0]		

Variable	CAVC (N=563)		CAVC without heterotaxy (N=345)		Isolated CAVC (N=47)	
	1999–2008 Adjusted prevalence ratio [95% CI <sup>a</sup> ]	2005–2008 Adjusted prevalence ratio [95% CI <sup>a</sup> ]	1999–2008 Adjusted prevalence ratio [95% CI <sup>a</sup> ]	2005–2008 Adjusted prevalence ratio [95% CI <sup>a</sup> ]	1999–2008 Adjusted prevalence ratio [95% CI <sup>a</sup> ]	2005–2008 Adjusted prevalence ratio [95% CI <sup>a</sup> ]
No		1.0 Reference		1.0 Reference		
Pre-gestational diabetes <sup>c</sup>						
Yes		6.7 [3.7, 12.4]		8.7 [3.9, 19.5]		
No		1.0 Reference		1.0 Reference		
Body mass index (kg/m <sup>2</sup> ) <sup>c</sup>						
Underweight (<18.5)		1.1 [0.5, 2.1]		1.1 [0.4, 3.1]		
Normal (18.5–24.9)		1.0 Reference		1.0 Reference		
Overweight (25.0–29.9)		1.3 [0.9, 1.8]		1.2 [0.8, 2.0]		
Obese (≥30)		1.7 [1.2, 2.3]		1.5 [0.9, 2.4]		

<sup>a</sup>CI, confidence interval

<sup>b</sup>Data were missing for 17.8% of cases for paternal age

<sup>c</sup>Data available for cases delivered in 2005–2008 only